Mathematical Models of Epidemics
The Covid 19

Etienne Pardoux (AMU)

joint work with G. Pang (U. Penn.) and R. Forien (INRAE)

Ascona Round Table

The classical SIR model

- It is one of the most popular models of epidemics. A population of fixed size N is distributed into 3 compartments : S = “susceptible”, I = “infectious”, R = “recovered” (and immune .. or dead).
- The deterministic ODE model for proportions reads

$$\frac{d\bar{S}}{dt}(t) = -\lambda \bar{S}(t)\bar{I}(t),$$
$$\frac{d\bar{I}}{dt}(t) = \lambda \bar{S}(t)\bar{I}(t) - \gamma \bar{I}(t),$$
$$\frac{d\bar{R}}{dt}(t) = \gamma \bar{I}(t).$$

λ = contact rate, γ = rate of curing.

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Is the above a good model ?

- Consider the equation for the number of infectious individuals

$$\frac{dI}{dt}(t) = \lambda \bar{S}(t) I(t) - \gamma I(t) \,.$$

- The idea : each infectious meets others at rate λ, which results in a new infection if the encountered individual is susceptible.
- The second term means that the duration of the infectious period is a r.v. with the $\mathrm{Exp}(\gamma)$ distribution.
- This assumption is quite unrealistic. Suppose that distribution has an arbitrary d.f. $F(t)$. Then, with $F^c(t) = 1 - F(t)$,

$$\bar{S}(t) = \bar{S}(0) - \lambda \int_0^t \bar{S}(s)\bar{I}(s)ds,$$

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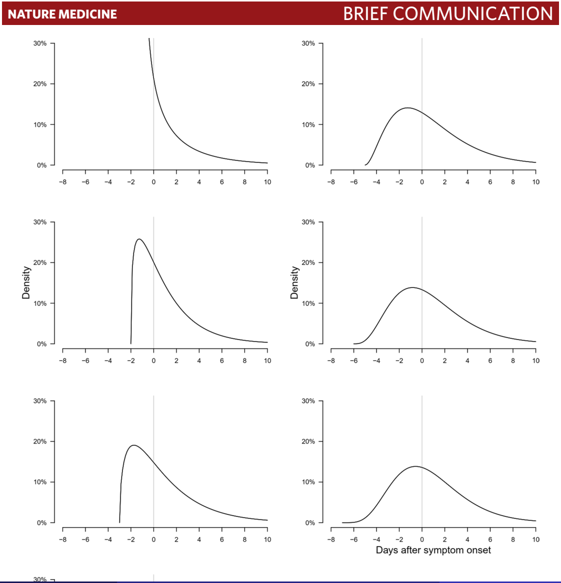
He, Lau, Wu et al., Nature Medicine 2020



Varying infectivity

- Let $\{\lambda(t),\ t \geq 0\}$ a random function with ≥ 0 values. If

  $$\mathcal{E} = \inf\{t > 0, \lambda(t) > 0\} \quad \mathcal{I} = \inf\{t > 0, \lambda(\mathcal{E} + t + r) = 0, \forall r > 0\}.$$

  Then $\mathcal{E}$ is the exposed period, $\mathcal{I}$ the infectious period.
  We assume that to each individual is attached a copy $\lambda_i(t)$, where the λ_i are i.i.d. To the initially infected individuals are attached copies $\lambda_j^0(t)$ of another type of infectivity function.
- We allow λ to have a finite given number of jumps, and assume uniform continuity between jumps. Then one can establish a law of large numbers as $N \to \infty$ of the corresponding individual based model. Define the total force of infection

  $$\mathfrak{I}^N(t) = \sum_{j=1}^{I^N(0)} \lambda_j^0(t) + \sum_{i=1}^{A^N(t)} \lambda_i(t - \tau_i^N),$$

  $$A^N(t) = \sum_{i \geq 1} \mathbf{1}_{(0,t]}(\tau_i^N) \text{ counts the number of indiv. infected on } (0, t].$$

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Varying infectivity : the LLN

- Let $S^N(t), I^N(t), R^N(t)$ denote resp. the number of susceptible, infected and recovered indiv. in the population. $S^N(t) + I^N(t) + R^N(t) = N$. For each process $X^N(t)$, we let $\bar{X}^N(t) := N^{-1}X^N(t)$.
- $(\bar{S}^N(t), \bar{\mathfrak{I}}^N(t), \bar{I}^N(t), \bar{R}^N(t)) \to (\bar{S}(t), \bar{\mathfrak{I}}(t), \bar{I}(t), \bar{R}(t))$ as $N \to \infty$, where, with $\bar{\lambda}(t) = \mathbb{E}[\lambda(t)]$, $\bar{\lambda}^0(t) = \mathbb{E}[\lambda^0(t)]$, $F =$ d.f. of $\mathcal{E} + \mathcal{I}$,

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The early phase of the epidemic

- We now replace $\lambda(t)$ by $\mu\lambda(t)$, where $\lambda(t)$ is the varying infectivity of any given individual, and μ measures the intensity of his/her social contacts. We can assume that $\lambda(t)$ is given to us by the medical science, while μ is essentially unknown, random and independent of λ, and is very much affected by measures like lockdown.
- Assume that we consider a phase during which $\bar{S}(t) \simeq 1$ (we could in fact consider any phase during which $\bar{S}(t) \simeq c$ for any c). We now let $(\mathfrak{I}(t), I(t), R(t)) \simeq (N\bar{\mathfrak{I}}(t), N\bar{I}(t), N\bar{R}(t))$ solution of

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The early phase of the epidemic. 2

- We look for a solution $\mathfrak{I}(t) = \iota e^{\rho t}$, $I(t) = \boldsymbol{i} e^{\rho t}$, $R(t) = \boldsymbol{r} e^{\rho t}$.
- Note that ρ is estimated from the data. We get

$$\bar{\mu} = \left(\int_0^\infty \bar{\lambda}(t) e^{-\rho t} dt \right)^{-1}, \iota = \rho, \boldsymbol{i} = \mathbb{E}[1 - e^{-\rho(\mathcal{E}+\mathcal{I})}], \boldsymbol{r} = \mathbb{E}[e^{-\rho(\mathcal{E}+\mathcal{I})}].$$

- We also have

$$R_0 = \frac{\int_0^\infty \bar{\lambda}(t) dt}{\int_0^\infty \bar{\lambda}(t) e^{-\rho t} dt}.$$

In the particular case where $\lambda(t) = \lambda \mathbf{1}_{[\mathcal{E}, \mathcal{E}+\mathcal{I})}(t)$,

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How R_0 depends upon the model

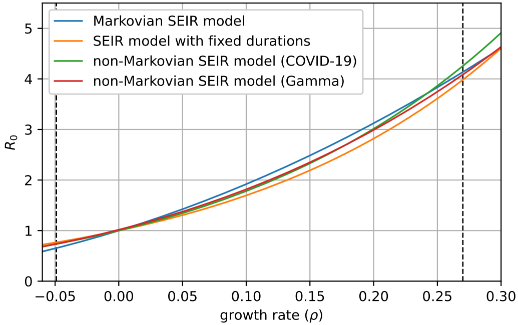

FIGURE – Value of R_0 as a function of the growth rate ρ for different distributions of the exposed and infectious periods $(\mathcal{E}, \mathcal{I})$. Four types of distributions are displayed : exponential (corresponding to the Markovian SEIR model), fixed, bimodal distribution mimicking Covid-19 (see below) and Gamma distribution. All distributions have a mean exposed time of 3 days and a mean infectious time of 4.8 days, corresponding to a proportion of reported individuals of 0.8.

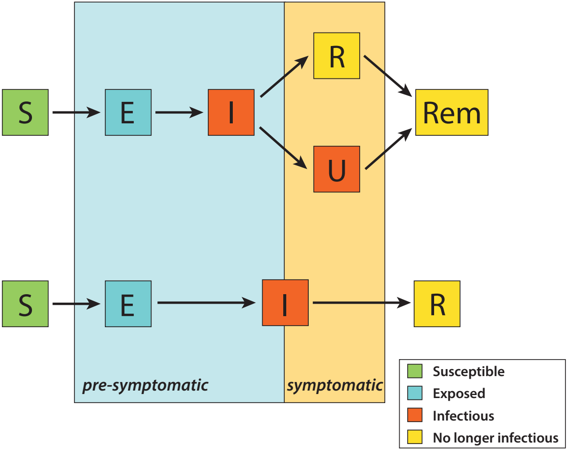

FIGURE – Flow chart of the SEIRU model of Liu, Magal et al. and the equivalent SEIR non-Markovian model. In the latter, I and U are merged into one compartment, also R and Rem are merged into one compartment.

The Covid epidemic. 2

- We let

$$\mathcal{E} = 2 + 2X_1$$

and

$$\mathcal{I} = Y(3 + X_2) + (1 - Y)(8 + 4X_3),$$

where X_1, X_2, X_3, Y are independent, X_1, X_2 and X_3 having a beta distribution on $[0, 1]$, Y is a Bernoulli r.v., with $0.2 \leq \mathbb{P}(Y = 1) \leq 0.8$.

- If we choose $\mathbb{P}(Y = 1) = 0.8$ (resp. 0.2), our estimate of R_0 is 4.2 (resp. 6) prior to lockdown in France, while are estimates for R_0 during lockdown is 0.73 (resp. 0.67).

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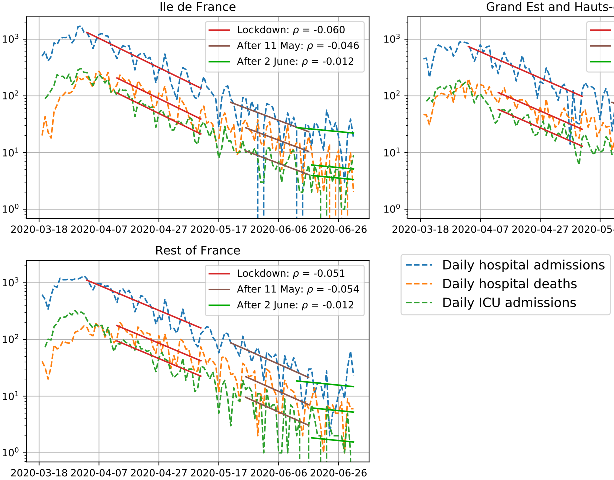
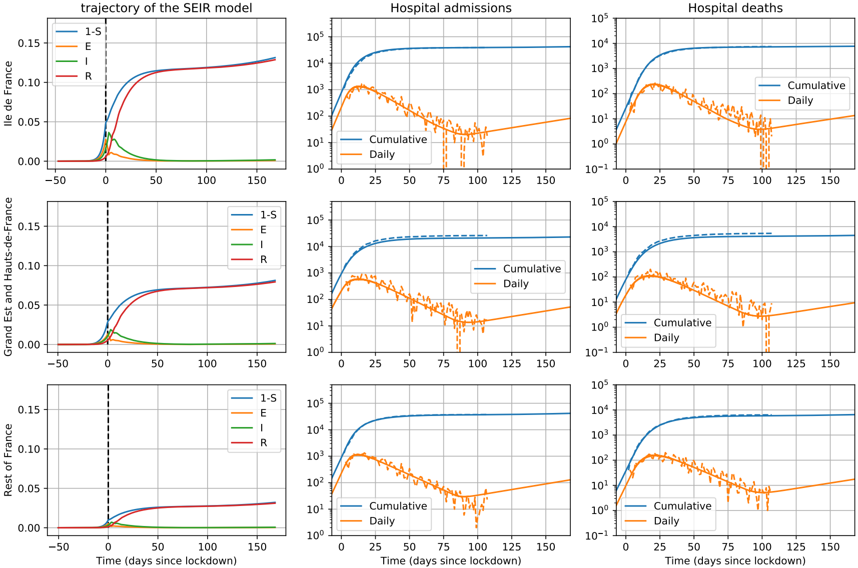
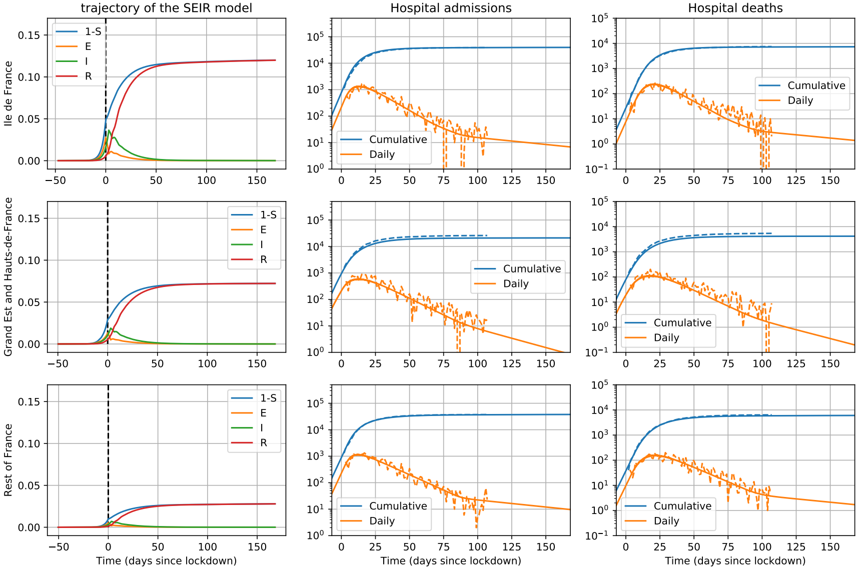
The Covid epidemic in France during and after lockdown



Prediction if $\rho = 0.02$ after June 2



More optimistic prediction



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THANK YOU FOR YOUR ATTENTION !